26. (New) A method according to claim 20, wherein the soluble RANK polypeptide consists of amino acids 30-213 of SEQ ID NO:2 fused with an amino acid sequence as shown in SEQ ID NO:3. --

REMARKS

Claims 1-24 are pending in the application and are subject to a Restriction Requirement that was issued 3/26/2002. As indicated above, Group III (claims 5-16, 18-20 and 22-24) has been elected for immediate prosecution. Claims 5, 9, 11, 13 and 15 have been amended and claims 6-8, 10, 12, 14, 19, 22, 23 and 24 have been cancelled from the application. New claims 25 and 26 have been added to the application as indicated above.

Applicants have amended the specification to incorporate a substitute Sequence Listing that includes the nucleotide and amino acid sequences of human RANKL, which have been designated as SEQ ID NOS:7 and 8, respectively. These RANKL sequences are disclosed in USSN 08/996,139 (now U.S. 6,017,729), which is incorporated by reference in the instant application at page 2, line 35 to page 3, line 1. The specification has also been amended at pages 4-5 to add a reference to SEQ ID NOS:7 and 8 and to specify that these sequences refer to human RANKL. Because the human RANKL sequences are disclosed in a publication that is incorporated by reference, the amendments to the Sequence Listing and specification do not constitute the addition of new matter to the application. Attached hereto are a paper copy of the substitute Sequence Listing and duplicate diskettes each containing an electronic copy of the substitute Sequence Listing.

As indicated above, applicants have amended claims 5, 9, 11, 13 and 15 to more particularly point out and distinctly claim what they regard as their invention. Support for these amendments are found in the claims as previously filed and throughout the specification.

The amendments to claims 5 and 13 are supported, for example, by cancelled claims 6-8, 10, 14, 22, 23 and 24, by the amendments to the specification and Sequence Listing, and throughout the specification, for example, at page 2, lines 5-12; page 3, lines 3-9; page 4, lines 20-36; and page 7, lines 15-24. Claim 9 is amended so that it now depends from claim 5 rather than from cancelled claim 8, but otherwise is unchanged.

Claims 11 and 15 are amended to depend, respectively, from claims 9 and 16 rather than cancelled claims 10 and 14. Further amendments to these claims recite

RANK amino acid sequences, as supported in the specification, for example, at page 3, lines 3-7.

New claims 25 and 26 have been added to the application and are supported by the Sequence Listing, the cancelled claims and the specification, such as at page 2, lines 13-17 and page 3, lines 3-7 and 15-18 and page 4, lines 30-32.

In view of the above remarks, none of the above amendments to the claims or specification constitute the addition of new matter to the application.

CONCLUSIONS

The above claims are believed to be in condition for allowance and notification to that effect is respectfully requested. To expedite prosecution of this application, the examiner is urged to contact the undersigned at her direct dial number given below to discuss any areas of concern regarding these claims.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this Response to Restriction Requirement and Third Preliminary Amendment is being deposited with the United States Postal Service as first class mail in an envelope addressed to: U.S. Patent and Trademark Office, P.O. Box 2327, Arlington, VA 22202, on the date indicated below.

Date: June 18, 2002

D. F. Lindholm

APPENDIX TO THIRD PRELIMINARY AMENDMENT
(marked-up version of paragraphs amended in the attached
Third Preliminary Amendment)

Specification:

Page 4, line 37:

The biological activity of RANK analogs or muteins can be determined by testing the ability of the analogs or muteins to bind human RANKL (SEQ ID NOS:7 and 8), for example as described in the Examples herein. Suitable assays include, for example, an enzyme immunoassay or a dot blot, and assays that employ cells expressing RANKL. Suitable assays also include, for example, inhibition assays, wherein soluble RANK is used to inhibit the interaction of RANKL with membrane-bound or solid-phase associated RANK (i.e., signal transduction assays). Such methods are well known in the art.

Claims:

5. (Twice amended) A method of ameliorating effects of excess bone loss, comprising administering a soluble RANK polypeptide composition to an individual at risk for excess bone loss, wherein said individual is at risk from or suffers from a condition selected from the group consisting of bone cancer, multiple myeloma, melanoma and breast cancer, and further wherein the soluble RANK polypeptide is capable of binding to a RANKL polypeptide that consists of amino acids 1-317 of SEQ ID NO:8 and is selected from the group consisting of:

(a) a polypeptide encoded by a DNA that encodes a protein comprising amino acids 33-196 of SEQ ID NO:2;

(b) a polypeptide encoded by a DNA that is capable of hybridizing to a DNA consisting of the nucleotide sequence shown in SEQ ID NO:1 under stringent conditions, wherein stringent conditions comprise hybridizing at 63°C in 6 x SSC;

(c) a polypeptide that is at least 80% identical in amino acid sequence to a RANK polypeptide comprising amino acids 1-213 of SEQ ID NO:2; and

(d) a polypeptide comprising amino acids 33-213 of SEQ ID NO:2.

9. (Once amended) The method of claim [8] 5, wherein the RANK further comprises a polypeptide selected from the group consisting of an immunoglobulin Fc domain, an immunoglobulin Fc mutein, a FLAG™ tag, a peptide comprising at least [about] 6 His residues, a leucine zipper, and combinations thereof.

11. (Once amended) The method of claim [10] 9, wherein the soluble RANK polypeptide comprises an amino acid sequence that is at least [about] 80% identical in amino acid sequence to [native RANK] amino acids 33-213 of SEQ ID NO:2.

13. (Once amended) A method of ameliorating the effects of excess bone loss comprising administering to a patient in need thereof a therapeutic composition comprising a recombinant soluble RANK polypeptide, wherein said patient suffers from a condition selected from the group consisting of squamous cell carcinoma, lung cancer, prostate cancer, hematologic cancer, head and neck cancer and renal cancer, and further wherein the soluble RANK polypeptide is capable of binding to a RANKL polypeptide that consists of amino acids 1-317 of SEQ ID NO:8 and is selected from the group consisting of:

(a) a polypeptide encoded by a DNA that encodes a protein comprising amino acids 33-196 of SEQ ID NO:2;

(b) a polypeptide encoded by a DNA that is capable of hybridizing to a DNA consisting of the nucleotide sequence shown in SEQ ID NO:1 under stringent conditions, wherein stringent conditions comprise hybridizing at 63°C in 6 x SSC;

(c) a polypeptide that is at least 80% identical in amino acid sequence to amino acids 1-213 of SEQ ID NO:2; and

(d) a polypeptide comprising amino acids 33-213 of SEQ ID NO:2.

15. (Once amended) The method of claim [14] 16, wherein the soluble RANK polypeptide comprises an amino acid sequence that is at least [about] 80% identical in amino acid sequence to [native RANK] amino acids 33-213 of SEQ ID NO:2.

16. (Once amended) The method of claim 13, wherein the soluble RANK polypeptide further comprises one or more polypeptides selected from the group consisting of an immunoglobulin Fc domain, an immunoglobulin Fc mutein, a FLAG™ tag, a peptide comprising at least [about] 6 His residues and a leucine zipper.